Citation:

Dickinson HO, Nicolson DJ, Campbell F, Beyer FR, Mason J. Potassium supplementation for the management of primary hypertension in adults. Cochrane Database Syst Rev. 2006 Jul 19;3.

PubMed ID: 16856053

Study Design:

Systematic Review/Meta-analysis

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the effects of potassium supplementation on health outcomes and blood pressure in adults with primary hypertension.

Inclusion Criteria:

- RCTs of a parallel or crossover design comparing oral potassium supplements with placebo, no treatment, or usual care
- Treatment and follow-up of eight weeks or more
- Oral potassium supplementation, or dietary inteventions which manipulated only potassium intake
- Participants over 18 years, with raised systolic blood pressure (SBP) equal or greater than 140 mmHg or diastolic blood pressure (DBP) equal or greater than 85 mmHg without a known primary cause
- SBP and DBP reported at the end of follow-up
- Crossover trials restricted to designs with 2 intervention and 2 treatment periods

Exclusion Criteria:

- Trials that included:
  - Pregnant women
  - Participants receiving antihypertensive medication which changed during the study
  - Participants with potassium supplementation combined with other interventions

Description of Study Protocol:

Recruitment:

- Databases searched included: Cochrane Library, MEDLINE, EMBASE, Science Citation Indes, ISI Proceedings, ClinicalTrials.gov, Current Controlled Trials, CAB abstracts
- The reference lists of systematic reviews and meta-analyses from these databases as well as randomised controlled trials were identified
- The search was based in a strategy where terms in capitals are MeSH headings, so the strategy could be developed within MEDLINE and adjusted accordingly for the other databases.
- In addition, a general web search using the search engines Google, Zapmeta and Dogpile, as well as web sites of the Blood pressure Association, British Hypertension Society, American Society of Hypertension, and Canadian Hypertension Society was carried out
- There was no language restriction
- Methodological quality of included trials was assessed considering these criteria: blinding (yes, no, unclear); randomization (adequate, inadequate or unclear); allocation concealment from treatment providers and participants (adequate, inadequate or unclear); loss to follow-up (recorded number of participants in each intervention arm whose blood pressure was not reported at the end of the study,or if loss of follow-up was not reported); carryover effects (for crossover trials, assessment of carryover effects at the end of follow-up and whether was reported)

Design: Systematic Review/Meta-analysis

Blinding used (if applicable): not applicable

Intervention (if applicable): Trials of potassium supplementation

Statistical Analysis:

- Separate meta-analysis of parallel and crossover trials were conducted, but they were combined if they did not show heterogeneity
- When standard deviations of final values were not available, they were imputed. In crossover treatment effect the standard deviation was imputed, assuming the mean within-person correlation observed in other crossover trials which evaluated the effect on blood pressure of oral supplements of calcium, sodium and magnesium
- Random effects model was perfomed using the meta-analysis combined with weighted mean diferences according to the precision of each trial.
- Heterogeneity between trials was assessed using the I^2-statistic
- Sub-groups analyses were performed, grouping the trials into those participants in the active arm received higher and lower doses of potassium, and participants' mean baseline blood pressure was higher and lower
- Sensitivity analysis were conducted excluding trials which did not report adequate concealment of allocation, blinding of participants, treatment providers and outcome assessors
- A post-hoc sensitivity analysis was performed, excluding one trial in an African population
- Additionally, post-hoc analyses were conducted to evaluate the effect of potassium supplementation on serum potassium levels
- Tolerability of intervention was assessed in the parallel trials by calculating the difference in the rate of withdrawal in the treatment and control arms, and using a random effects model to calculate a pooled risk difference

- Gastrointestinal effects were assessed by calculating the difference in the rate of these effects in treatment and control arms, and using a random effects model to calculate a pooled risk difference

Data Collection Summary:

Timing of Measurements: not applicable

Dependent Variables

- SBP at end of follow-up
- DBP at end of follow-up
- Fatal or non-fatal myocardial infarction
- Fatal or non-fatal strokes
- Death from all causes

Independent Variables

- Potassium supplementation - participants who received more than 100 mmol/day (active treatment arm) or equal or less than 100 mmol/day (control arm)

Control Variables

Description of Actual Data Sample:

Initial N: initial screening was 1,282; retrieved was 48 RCTs

Attrition (final N): 5 RCTs; 425 participants

Reasons for exclusion: 42 RCTs excluded at paper screening stage; 1 RCT excluded from meta-analysis) follow-up less than eight weeks (18 trials); normotensive participants (11 trials); antihypertensive medication varied during the trial (4 trials); intervention consisted of multiple supplements (2 trials); survey study desing (2 trials); follow-up less than eight weeks and normotensive participants (1 trial); participants not randomly allocated to the sequence of treatment (1 trial); observational study (1 trial), control group on drugs (1 trial); trial of multiple interventions (1 trial), and combined increased potassium with decreased sodium intake (1 trial)

Age: mean age was 50 years (range:36-52 years)

Ethnicity: reported from only two trials which was 61% white

Other relevant demographics: Overall 75% of the participants were male. Little information was reported about the normal diet of participants.

Anthropometrics: none specified

Location: USA, Australia, Kenya, Germany and Italy

Summary of Results:

Key Findings

- Six RCT's (n=483), with 8-16 weeks follow-up, met the inclusion criteria
- Meta-analysis of five trials (n=425) with adequated data indicated that potassium supplementation compared to control resulted in a large but statistically non-significant reduction in SBP (mean difference: -11.2,95%CI:-25.2 to 2.7) and DBP (mean difference:-5.0, 95%CI:-12.5 to 2.4). The substantial heterogeneity between trials (I^2 =98% and 99% for SBP and DBP respectively) was not explained by potassium dose, quality of trials or baseline blood pressure
- Excluding one trian in an African opulation with very high baseline blood pressure resulted in smaller overal reductions in blood pressure (SBP mean difference: -3.9,95%CI:-8.6 to 0.8; DBP mean difference: -1.5, 95%CI:-6.2 to 3.1)
- Two trials administering lower (≤ doses of potassium showed greater reductions in BP than three trials administering ≥ 100 mmol per day, which was significant for DBP (mean differences in the two trials = -17.00 (95% CI: -19.25, -14.75) and -10.50 (95%CI: -16.32, -4.68) mmg Hg)
- Sensitivity analysis of two high quality trials found overall reduction in blood pressure among participants taking potassium supplementation remained non-significant for both SBP (mean difference: -7.1, 95%CI: -19.9 to 5.7) and DBP (mean difference: -5.5,95%CI:-14.5 to 3.5). There was considerable heterogeneity between the trials (I^2= 87% for both SBP and DPB).

Other Findings

- No trials reported deaths or cardiovascular events. Only one trial reported adverse effects in both control and treatment groups,with more stomach pains and flatulence in the potassium-treated group
- Overall mean blood pressure at baseline was 151/95 mmHg (SBP range:145-174 mmHg; DBP range:92-100 mmHg)
- The dose of potassium supplementation varied from 48 and 120 mmol/day
- Meta-analysis showed no significant difference in the rate of withdrawal between the treatment groups (risk difference=-0.03, 95%CI: -0.07 to 0.02
- Overall participants receiving potassium supplementation had higher serum potassium levels at the end of the trials than the controls (mean difference:0.20 mmol/l, 95%CI:0.02 to 0.38)
- The funnel plot analysis of estimated treatment effects for SBP and DPB showed little evidence of publication bias

Author Conclusion:

Potassium supplementation has no statistically significant effect on blood pressure. Due to small number of participants in the two high quality trials, the short duration of follow-up, and the unexplained heterogeneity between trials, the evidence about the effect of potassium supplementation on blood pressure is not conclusive. Further high quality RCTs of longer duration are required to clarify whether potassium supplementation can reduce blood pressure and improve health outcomes.

Reviewer Comments:

The majority of studies were not of good quality, with the exception of two trials. Substantial heterogeneity was found among the studies which can compromise the outcomes. There was an over representation of males in most of the trials included in this review.

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity Questions		
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	No
10.	Was bias due to the review's funding or sponsorship unlikely?	Yes